Registration Decision RD2014-06

Metrafenone

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Registration Decision for Metrafenone

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Metrafenone Technical Fungicide and Vivando SC Fungicide, containing the technical grade active ingredient metrafenone, to control powdery mildew on grapes.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2013-07, *Metrafenone*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for metrafenone and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2013-07. This decision is consistent with the proposed registration decision stated in PRD2013-07.

For more details on the information presented in this Registration Decision, please refer to PRD2013-07, which contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What is Metrafenone?

Metrafenone is a benzophenone fungicide with protectant and curative properties for the control of powdery mildew (*Uncinula necator*) on grapes.

Health Considerations

Can Approved Uses of Metrafenone Affect Human Health?

Potential exposure to metrafenone may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when metrafenone products are used according to label directions.

In laboratory animals, the technical grade active ingredient is of low acute oral, dermal and inhalation toxicity, is non-irritating to the skin, not a dermal sensitizer, and is minimally irritating to the eyes. The end-use product, Vivando SC Fungicide, is of low acute oral, dermal and inhalation toxicity, is non-irritating to the skin, and is not a sensitizer. The end-use product is mildly irritating to the eyes. Consequently, the signal words "CAUTION – EYE IRRITANT" are required on the label of the end-use product.

Metrafenone was not genotoxic and not likely to pose a carcinogenic risk to humans. There was also no indication that metrafenone caused damage to the nervous system. Common effects of toxicity in animals given daily doses of metrafenone over longer periods of time were changes to the kidneys and liver, irritation to the ear, and effects on the blood indicative of regenerative anaemia.

When metrafenone was given to pregnant animals, effects on the developing fetus, such as decreased body weight compared to controls and an increase in early fetal loss, were only observed at doses that were toxic to the mother, indicating that the fetus is not more sensitive to metrafenone than the adult animal.

The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children 1-2 years old, (the subpopulation that would ingest the most metrafenone relative to body weight), are expected to be exposed to less than 2% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from metrafenone is not of concern for all population subgroups.

Animal studies revealed no acute health effects. Consequently, a single dose of metrafenone is not likely to cause acute health effects in the general population (including infants and children).

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established Maximum Residue Limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

The analytical methodology data submitted to support the conversion from conditional to full registration are adequate.

Occupational Risks From Handling Vivando SC Fungicide

Occupational risks are not of concern when Vivando SC Fungicide is used according to the label directions, which include protective measures.

Farmers and pesticide applicators who mix, load or apply Vivando SC Fungicide, as well as field workers entering freshly treated fields, can come in direct contact with Vivando SC Fungicide residues on the skin or through inhalation of spray mists. Therefore, the label specifies that anyone mixing/loading and applying Vivando SC Fungicide must wear long-sleeved shirt, long pants, chemical-resistant gloves, socks and footwear. The label also requires that workers do not enter treated fields for four days after application to perform girdling or cane turning and 12 hours for all other postapplication activities. Taking into consideration these label statements, the number of applications and the expectation of the exposure period, risks for farmers and applicators are not a concern.

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Metrafenone Is Introduced Into the Environment?

Metrafenone enters the environment when used as a fungicide on grape crops. Metrafenone is toxic to some non-target aquatic organisms. It is persistent in aerobic soil and is expected to carryover. Metrafenone is not persistent in anaerobic soil or in water, and it does not form any transformation products of environmental concern. Metrafenone is not expected to reach groundwater. Label instructions including spray buffer zones are required during pesticide application and handling.

Metrafenone is persistent in the terrestrial environment and displays low soil mobility. Based on field studies, approximately 40-45% carryover into the next growing season may be expected in soil. Metrafenone is sparingly soluble in water and is stable to hydrolysis. Despite these characteristics, it is not persistent in the aquatic environment. Many minor transformation products are formed, however, they do not pose an environmental concern because they are transient in nature and their concentrations are low. Due to low volatility (volatile organic compounds were not detected in the volatility traps used in laboratory incubation studies), metrafenone residues are not expected in the air, nor is long-range aerial transport expected. Leaching to groundwater is not a concern for metrafenone. It is not expected to bioaccumulate. Specific instructions to prevent soil carryover into the next growing season and runoff into aquatic habitats are provided on the end-use product label.

Metrafenone poses a negligible risk to the non-target terrestrial invertebrates tested including earthworms, honeybees, and beneficial arthropods. It also poses a negligible risk to the terrestrial vertebrates tested, including birds and small mammals. Although it displays low toxicity to terrestrial plants, there is some uncertainty regarding risk to plants owing to low application test rates. For freshwater organisms inhabiting waters close to 1 m in depth (80 cm deep or greater), metrafenone poses a negligible risk to all species tested. These include daphnids, chironomids, cold water fish (juvenile and early life stages), warm water fish (juvenile life stages), green algae, blue green algae, diatoms and aquatic vascular plants. However, metrafenone may pose an acute and chronic risk to amphibians inhabiting shallow waters (15 cm or less in depth). On an acute basis, metrafenone poses a negligible risk to estuarine/marine species including mysid shrimp, eastern oyster, and marine algae (represented by diatoms). It may pose a risk to marine fish (represented by sheepshead minnow) on an acute basis. On a chronic basis, it may pose a risk to mysid shrimp. Although the level of concern was exceeded for amphibians (acute and chronic), sheepshead minnow (acute), and mysid shrimp (chronic), proposed precautionary measures including label statements and spray buffer zones (1–2 m in size) are expected to adequately mitigate risk resulting from drift of metrafenone into the habitats of these sensitive organisms.

Value Considerations

What Is the Value of Vivando SC Fungicide?

Vivando SC Fungicide is a broad spectrum fungicide with strong activity against powdery mildew.

Vivando SC Fungicide is to be used to control powdery mildew on grapes. There are several alternative modes of action registered for control of this disease, two of which are strobilurin fungicides, with high risk of development of pest resistance. Metrafenone has a different mode of action that will aid in resistance management when used as a component in a fungicide spray program.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions are required by law to be followed.

The key risk-reduction measures on the label of Vivando SC Fungicide to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with Vivando SC Fungicide on the skin, anyone mixing, loading and applying Vivando SC Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and footwear during mixing/loading, application, clean-up and repair.

Environment

No new risk-reduction measures are required for the environment as a result of the new data submitted for the full registration of metrafenone and its associated end-use product. The label for the end-use product includes appropriate risk reduction measures.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2013-07, *Metrafenone)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, healthcanada.gc.ca/pmra) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.